

has been no rejection of the claims based on the use of that term in the claims. Thus, the amendments above are not made in response to a rejection.

Responding to a rejection of the claims based on the claim term "functional derivatives," applicants previously noted that the term "functional derivatives" in the claims literally encompasses chemically derivatized polypeptides (see, e.g., pages 11 to 13 of the specification), rather than amino acid substitutions, deletions, or insertions. See the Amendment filed May 14, 1997, e.g., at the paragraph bridging pages 14 and 15.

Applicants also discussed the newly added claims that included the term "variant" (a term that literally encompasses amino acid substitutions, deletions, or insertions). See *Id.* at page 15, first full paragraph, to page 16, first full paragraph. Those remarks were presented in an effort to expedite prosecution in the event the Examiner objected to the newly added term "variant." For at least those reasons, any rejection of claims including the term "variant" would be improper. However, since that claim term has been deleted to expedite prosecution, this issue is now moot.

Applicants have also amended the claims such that the term "fragment" has been replaced with the term "C- and/or N- terminally shortened sequence." During the interview and confirmed in the Examiner Summary Statement, Examiner Draper expressed concerns about modifications that she considered not to be enabled, indicating that the term "fragment" would encompass multiple internal deletions rather than only C- and/or N- terminally shortened sequences. Solely to expedite prosecution, the claims have been amended to recite such shortened sequences. Support for this amendment is found throughout the specification, e.g.,

at the paragraph bridging pages 27 and 28. Applicants respectfully assert that it would not take undue experimentation to make such shortened versions of the recited sequences in order to determine if such shortened sequences maintained the ability to bind to TNF.

Applicants have also amended or added claims to include specific N-terminal and/or C-terminal amino acid sequences or DNA sequences encoding such amino acid sequences. The specification fully supports these sequences.

For example, certain sequences include Asp-12 of Figure 1 at the N-terminus of the specific amino acids depicted. Those embodiments are supported throughout the specification, e.g., at the paragraph bridging pages 24 and 25.

Certain sequences include Leu-1 through Arg-11 of Figure 1 preceding Asp-12. Those embodiments are supported throughout the specification, e.g., at the sentence bridging pages 24 and 25.

Certain sequences include Asn-172 of Figure 1 at the C-terminus of the specific amino acids depicted. Those embodiments are supported throughout the specification, e.g., at page 25, first full sentence.

Certain sequences include Val-173 to Thr-182 of Figure 1 following Asn-172. Those embodiments are supported throughout the specification, e.g., at page 26, first paragraph. Specifically, that paragraph states that "[t]he region between Val-183 and Met-204 is strongly hydrophobic by nature. The paragraph goes on to note that such a hydrophobic region "followed by a portion containing positively charged amino acids . . . has the typical features of a transmembrane domain which anchors proteins in the cell membrane." Accordingly, the

specification conveys the possibility of a sequence comprising Val-173 to Thr-182 of Figure 1 following Asn-172.

Certain sequences include Met-S1 to Gly-S29 of Figure 1 preceding Leu-1. Those embodiments are supported throughout the specification, e.g., at the paragraph bridging pages 24 and 25.

Certain sequences include Met-S1 to Gly-S29 of Figure 1 preceding Asp-12. Those embodiments are supported throughout the specification, e.g., at page 36, lines 27-30.

Certain sequences include Met at the N-terminus of the specific sequence recited in the claim. Those embodiments are supported throughout the specification, e.g., at page 29, lines 30-31.

During the interview, Examiner Draper expressed concerns about the claims directed to nucleic acid that hybridizes to DNA complementary to DNA defined in claim 1 under conditions of low stringency. For the reasons set forth in the Amendment filed May 14, 1997, applicants continue to maintain that low stringency conditions would be understood by those skilled in the art and would not include conditions under which unrelated nucleic acids would be obtained. Solely to expedite prosecution and not acquiescing in any rejection, applicants have amended the claims directed to hybridizing nucleic acids to require moderate stringency. Applicants assert that one skilled in the art would understand what is encompassed by moderately stringent conditions, such as the conditions set forth in Example 10 of the present specification.

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Also, applicants note that the Examiner Summary indicated that Examiner Draper considers claims directed to conservative modifications acceptable. Accordingly, in the Supplemental Amendment, applicants added claim 87 that includes the term "conservative amino acid substitution", which is a modification of an amino acid sequence of a polypeptide having the ability to bind to TNF, such that the modified polypeptide retains TNF binding properties.

Applicants also address an assertion of the Examiner in the Office Action mailed November 14, 1997. In the Action, the Examiner contended that the specification equated the TNF-BP in the specification to a protein discussed in EP-A2 308 378. Applicants point out that the portion of the specification cited by the Examiner (page 9, lines 20-22) compares the TNF-BP purified from urine in the specification to material obtained from urine in EP-A2 308 378. That statement does not compare recombinantly produced TNF-BP to material obtained from urine in EP-A2 308 378.

Also during the interview, additional copending applications of Hauptmann et al. and applications of Brewer et al. were discussed. Presently, the following additional Hauptmann et al. applications are pending: U.S. Serial Nos. 08/383,676; 08/477,638; 08/477,639; and 08/484,307. Also the following Brewer et al. applications are pending: U.S. Serial Nos. 08/375,242; 08/484,337; and 08/485,439 (this last application was abandoned and petition to revive has been filed). (Brewer et al.'s U.S. Application Serial No. 08/092,538 recently was abandoned.) The present application and all of the Hauptmann et al. applications listed above and the Brewer et al. applications listed above are presently both assigned to Synergen, Inc.

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It is the understanding of Paul Barker that the Hauptmann et al. applications were not assigned to Synergen, Inc. at the time of the invention in the Hauptmann et al. applications.

When the present application and Serial Nos. 08/477,638, 08/477,639, and 08/484,307 were filed, the Rule 60 forms of each application erroneously indicated that the parent application (U.S. Serial No. 08/383,676) had been assigned to Amgen Acquisitions Subsidiary, Inc. The parent application in fact was assigned to Synergen, Inc., and thus the continuation or divisional applications are also assigned to Synergen, Inc. Synergen, Inc. has become a subsidiary of Amgen Inc. The Brewer et al. applications, the present application, and the Hauptmann et al. applications still are assigned to Synergen, Inc. Synergen, Inc.'s name has been changed to Amgen Boulder Inc., and that name change has not yet been recorded at the U.S. Patent and Trademark Office.

As discussed at the interview, applicants intend to pursue separately patentable subject matter in the Hauptmann et al. applications on the one hand and the Brewer et al. applications on the other hand. The claims presented above are directed to subject matter that applicants believe the Hauptmann et al. applications are entitled to in view of the effective invention dates of the Hauptmann et al. applications in relation to the effective invention dates of the Brewer et al. applications.

Applicants request that Examiner Draper consider the comments in this Supplemental Amendment when she considers this application. Also, applicants request that Examiner Draper call the undersigned at (202) 408-4067 if she believes that a discussion would further advance prosecution of this case.

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If there are further fees due in connection with the filing of this Amendment, such as fees under 37 C.F.R. §§ 1.16 or 1.17, please charge the fees to our Deposit Account No. 06-0916. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested. This fee also should be charged to our Deposit Account No. 06-0916. Any overpayment may be credited to Deposit Account No. 06-0916.

Respectfully submitted,

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By:



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